## REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the following remarks.

### ACKNOWLEDGMENT OF FOREIGN PRIORITY

Applicants request that the Examiner acknowledge applicants' claim for priority of FR 02/14534, filed November 20, 2002; a certified copy was filed herein on May 25, 2004.

### STATUS OF CLAIMS

Claims 1, 2, 4-7, 9-12, 15, 16, 18-23, 36, 38-44, 46-49 and 53-60 remain in the application. Claims 9, 10, 21 and 48 have been withdrawn from consideration.

The independent claims have been amended to limit the compound applied to either (a) a very narrow group of compounds of formula (I) or their salts in which the definition of $R_1$ and $R_2$ has been limited as in previous Claim 14, which has now been cancelled as redundant; or to the specific compound which is depicted as Compound 2 in Claim 22. The narrow genus of formula (I) in the independent claims encompasses the compound depicted as Compound 1 in Claim 22 and other compounds very closely related structurally to Compound 1, including the compounds depicted as Compounds 3 and 5-8 in Claim 22. Formula (I) has also been redrawn to use subscripts for the various R groups, consistent with the definitions in the claims.

Claim 4 has been amended to recite "reducing" and "reduction" rather than "inhibiting" and "inhibition", respectively, so as not to imply that the lessening of 15-PGDH is total.

Claim 5 has been amended to recite alopecia rather than a 15-PGDH disorder.

In Claim 22, Compound 4 has been deleted as not falling within amended Claim 1.

Minor other claim amendments have been made in the way of clarifications and corrections.

None of the amendments introduce new matter into the application. These amendments have been made in an effort to expedite prosecution. However, applicants do not concur with the Examiner's enablement rejection herein and specifically reserve the right to pursue broader claims in a continuing application.

WITHDRAWN REJECTIONS

The withdrawal of the previous 35 U.S.C. § 103(a) rejections is noted with appreciation.

CLAIM REJECTIONS - - 35 U.S.C. § 112, FIRST PARAGRAPH

All of the examined claims have been rejected under 35 U.S.C. § 112, first paragraph, because the specification:

(1) purportedly does not reasonably provide sufficient enablement of a seemingly infinite number of ingredients to induce hair growth and increase hair density by inhibiting 15-PGDH without an undue amount of experimentation;

(2) is enabling for alopecia but purportedly not all 15-PGDH disorders;

(3) is purportedly not enabling for complete inhibition of 15-PGDH but only of reduction therefor.

Applicants submit that the Examiner's reasons for finding lack of enablement cannot be maintained against the claims now in this application.

Specifically, with respect to point (1) above, the compounds are now very narrowly defined. There is not a seemingly infinite number of derivatives encompassed by the claims. The scope of formula (I) is very limited and includes only compounds sharing a commonality of substituents with Compound 1, for which data is included in the specification. These compounds are very closely related structurally to Compound 1 and are indeed specifically exemplified by the structures of Compounds 3, 5, 6, 7 and 8 so that there would be no undue amount of experimentation involved in arriving at other suitable derivatives. As to part (b) of the generic claims, a single compound, Compound 2, is encompassed thereby and data has been presented for it in the specification as well.

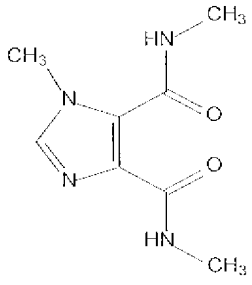
With respect to point (2), Claim 5 has been limited to treatment of alopecia, which obviates this part of the enablement rejection.

With regard to point (3), applicants have amended Claim 4 so that it refers to reduction rather than inhibition, rendering this portion of the enablement rejection moot as well.

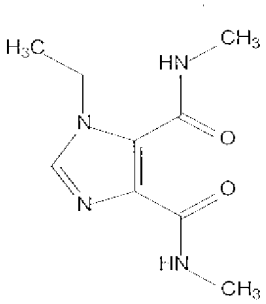
With regard to the level of predictability in the art and the state of the art, applicants submit that one of ordinary skill would certainly expect the compounds now encompassed by the generic claims to have the properties applicants ascribes to them, based on the synthetic and biological data present in the specification, and that skilled person could easily synthesize and test additional compounds within the claimed genus without undue experimentation. Furthermore, the examples the Examiner has given of unpredictability in the art do not relate to compounds substantially similar in structure to those here claimed and therefore are irrelevant to the present case.

More particularly, the Examiner has indicated that unpredictable and surprisingly dramatic effects can result from a simple modification of a compound, using opiod analgesics and inhibitors of Cathepsin D as examples. Applicants submit that the predictability or lack of predictability of structural changes in opiod analgesics and inhibitors of Cathepsin D are not related to the present application. Applicants' compounds are unrelated to opiod analgesics and inhibitors and Cathepsin D in structure so as well as activity. What may be true of opiod-type structures or of an aspartylprotease is irrelevant to the case at hand. Further, the Examiner has mischaracterized her analysis of the article on inhibitors of Cathepsin D.

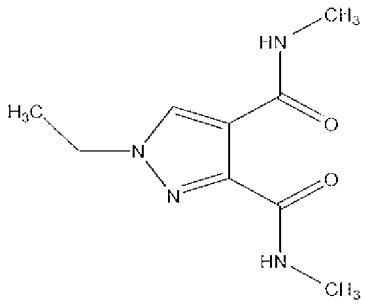
The Examiner has also cited several references (one journal article in Russian, two U.S. patents and a published U.S. patent application) dealing with "substituted pyrazolecarboxamide" derivatives as showing these compounds have marked different properties purportedly due to their substituents. The Examiner cites the Abstract of the journal article (Bogoslovskaia) which evaluated the effects of alkyl derivatives of imidazoledicarboxylic acid diamides on respiration and acid-base balance of animals. The three compounds listed in the abstract are shown below, with their structures.




Antiphcin




Ethymisole




Ethirazol

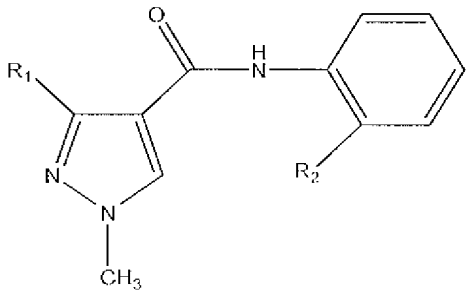
The abstract discloses that antiphein and ethymisole stimulate respiration and change the acid-base balance, while ethirazol does not affect respiration and also states:

> Differences in the biological activity of the test drugs may be related to the structure or position of the alkyl radical in the heterocyclic ring.

The Examiner cites this as an example of the unpredictability of a simple modification on the biological activity of substituted pyrazolecarboxamide. However, the Bogoslovskaia compounds are very special pyrazolecarboxamides; they are in fact invariably pyrazole or imidazole dicarboxylic acid diamides, a possibility which applicants compounds do not encompass. Furthermore, more than a change in the position of the radical in the heterocyclic ring is involved, as the two compounds with similar properties are imidazoles, while only ethirazole is a pyrazole derivative. Applicants' compounds are invariably pyrazole monocarboxylic acid amides, moreover, applicants' compounds cannot contain a simple $CONHCH_3$ as their $CONR_1R_2$ grouping, whereas such is the only amide structure shown by the Russian reference.

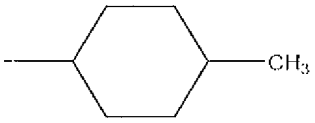
The Examiner has also cited two patents and one patent application for purportedly showing that the properties of a compound vary with the substituents on the core.

McLoughlin et al. US 5,498,624 is directed to 2'-(substituted)cyclohexyl carboxanilides of the formula below, which are useful as fungicides:

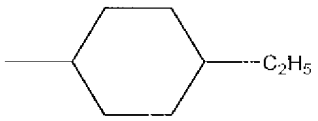


wherein:

$R_1$ is $CF_3$ and $R_2$ is

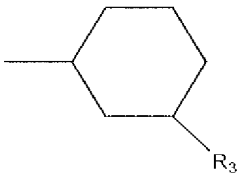


or



or

$R_1$ $CHF_2$ and $R_2$ is



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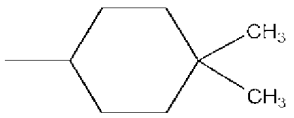
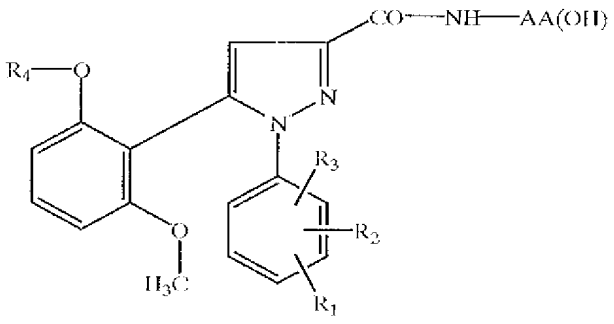


wherein

$R_3$ is $CF_3$ or $CH_3$; $R_4$ is $CH_3$, $C_2H_5$, $CF_3$ or $OC_2H_5$; and $R_5$ is H or $CH_3$.

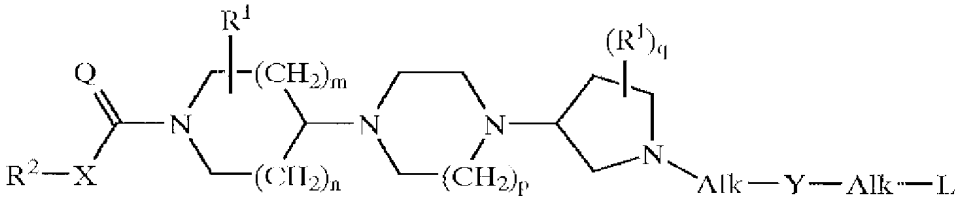
Thus, the "core" of the '624 compounds encompasses a phenyl-substituted amide and the amide itself encompasses a cyclohexyl ring at the 2-position. Applicants' compounds cannot contain a phenyl-substituted amide. The '624 compounds are structurally distinct and are useful as fungicides; they are irrelevant to the compounds claimed herein, both in terms of structure and in terms of utility.

Labeeuw et al. US 5,965,579 is directed to 1-phenyl-3-pyrazolecarboxamides having the formula below, which are active on neurotensin receptors:



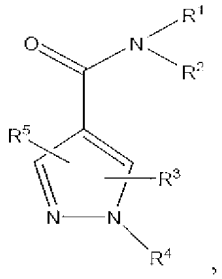

These compounds invariably contain as part of their "core" the amide grouping -CONHAA(OH), the AA(OH) representing an amino acid. There is no such amino acid-substituted amide group in applicants' compounds. Applicants' compounds are structurally distinct, and the '579 patent is irrelevant.

Janssens et al. US 2006/0040950 is directed to substituted 1-piperidin-4-yl-4-pyrrolidin-3-yl-piperazine derivatives having the following formula, which are neurokinin antagonists:




The '950 compounds have virtually nothing in common with applicants' compounds. There is no pyrazole ring (an unsaturated ring), indeed, all rings are fully saturated. These compounds have no common core with the compounds of the present invention.

The Examiner alleges that although US '624, US '579 and US '950 share the same core,



the properties displayed by each respective compound is markedly different due to the substituents. However the Examiner is mistaken in her conclusions because as just shown, the compounds of these references do not have the same "core" structure as herein. In the case of the '624 and '579 patents, the "core" in each case is different because they require very particular amide groupings not encompassed herein.

Also, the compounds of US 2006/0040950 do not have the "same core" as alleged by the Examiner because they do not even contain a pyrazole ring, as required by the Examiner's core structure and as required by applicants' structures. Therefore, the Examiner's conclusions are not supported.

In view of the foregoing, applicants submit that the record 35 U.S.C. § 112, first paragraph, rejection is untenable and should be withdrawn. Further, favorable action in the form of a Notice of Allowance is believed to be next in order and is earnestly solicited.

Respectfully submitted,

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